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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte
IDDYS D. FIGUEROA, VANESSA I. CHINEA, ORLANDO RUIZ, DOUGLAS A. SEXTON, WINTHROP D. CHILDERS, JAMES W. AYRES, and JOHN STEPHEN DUNFIELD

Appeal 2008-2962
Application 10/801,381
Technology Center 1700

Decided: August 28, 2008

Before TONI R. SCHEINER, DEMETRA J. MILLS, and LORA M. GREEN, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1-10 and 29-33. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

The claims are directed method of controlling the dissolution rate of a bioactive substance by applying the bioactive substance as a dot to a delivery substrate. Claim 1 is representative of the claims on appeal, and reads as follows:

1. A method of controlling a dissolution rate of a bioactive agent, the method comprising:

identifying a target dissolution rate;

applying a first drop of solution carrying the bioactive agent at a first selected location on a delivery substrate; and

positioning a second drop of solution carrying a bioactive agent at a second selected location on the delivery substrate, wherein the location of the first drop and the location of the second drop are selected based on the target dissolution rate.

The Examiner relies on the following references:

Voss	US 4,322,449	Mar. 30, 1982
Voges	US 5,894,841	Apr. 20, 1999

We affirm.

ISSUE (Obviousness over Voss)

The Examiner contends that claims 1-3, 6-10, and 29-33 are obvious over Voss (Ans. 4).

Appellants contend that the Examiner has failed to set forth a prima facie case of obviousness (App. Br. 7).

Thus, the issue on Appeal is: Has the Examiner set forth a prima facie case that claims 1-3, 6-10, and 29-33 are obvious over Voss.

FINDINGS OF FACT

FF1 The Specification teaches that "[d]rugs with a narrow therapeutic range must be precisely dosed in order to be safe and effective. If a recipient takes less than the effective dose, the desired effect will likely not occur. On the other hand, if the recipient takes more than the effective dose, the risk of toxic effects increases." (Spec. 2.)

FF2 According to the Specification:

> The ability to customize the release profile of a pharmaceutical can be advantageous. For example, if an active ingredient can be released so that the concentration of the active ingredient remains within a therapeutic range in a recipient's body over a 24 hour period, the recipient need only take the pharmaceutical once every day. As another example, some pharmaceuticals may be most effective when almost instantaneously absorbed by the recipient. Therefore, increasing the dissolution rate of the active ingredient can improve efficacy of the pharmaceutical. Traditional dosage forms and manufacturing techniques are characterized by limited control of the dissolution rates of the active ingredients when the dosage form is taken by a recipient. Therefore, controlling the release profiles of such drugs is difficult. Furthermore, fast release profiles associated with high dissolution rates are difficult to achieve.

(Spec. 3.)

FF3 The Specification teaches that prior methods of increasing dissolution rate have relied on physical grinding of the drug to yield micron and smaller

particles, or the use of spray-drying or freeze-drying to generate small particles to increase drug dissolution rates (Spec. 3).

FF4 The Specification thus teaches the use of a depositing system in the form of an ejection cartridge which can deliver the bioactive agent in the form of an ejection drop onto a delivery substrate, wherein the size, geometry, and other aspects of the ejection nozzle may be configured to eject drops of a desired volume (Spec. 8).

FF5 According to the Specification, "the geometric surface area of a dot can affect attributes of the bioactive agent, such as [the] dissolution rate of the bioactive agent." (Spec. 10.) The Specification teaches further that as demonstrated by the Noyes-Whitney equation, dissolution rate is directly proportional to surface area (Spec. 12). Thus, "the ability to control deposition characteristics can provide a high level of control over the attributes of the dosage form, such as the dissolution rate of the bioactive agent on the dosage form." (*Id.*) For example, a small dot size can increase surface-to-mass ratio, and subsequently increase the dissolution rate (*id.* at 15). Moreover, the desired dissolution rate can be determined through experimentation, in which application parameters such as drop size are varied until a desired dissolution rate is achieved (Spec. 20).

FF6 Claims 1-3, 6-10, and 29-33 stand rejected under 35 U.S.C. § 103(a) as being obvious over Voss (Ans. 4).

FF7 Voss is relied upon for teaching "a method of applying a bioactive agent to a delivery substrate in the form of dots forming a desired geometric[ ] pattern (See Abstract; col. 5, lines 35-37)." (Ans. 4.) Voss is further relied upon for teaching "the control of various parameters, such as

dots/second, volume/drop, concentration of the bioactive, number of ejection strokes, etc (1:60-65; 4:1-26, 6:1-7)." (*Id.*)

FF8 The Examiner finds that "[a]s is known in the art and as taught in the specification, controlling the dot pattern, the size or shape of the dot, or the consistency of the size of the dots will inherently provide control over the dissolution rate. The precise nature of Voss' printing technique yields such control." (*Id.*)

FF9 The Examiner finds as to the claim limitation of "identifying a target dissolution rate" that the safe and effective administration of a bioactive agent, such as a drug, "requires a precise dose at an acceptable 'target' dissolution rate," and that the ordinary artisan, such as medical professionals (doctors, pharmacists, and pharmaceutical company scientists) would understand that "a too-rapid dissolution rate could lead to an over-dose, whereas a too-slow dissolution rate could lead to ineffective treatment levels." (Ans. 4.) Moreover, according to the Examiner, "many medications are provided in a controlled release (CR) form to provide the correct dose over a period of time, inherently requiring the use of a target dissolution rate." (*Id.*)

FF10 Specifically, Voss teaches that active substances who are dosed in small doses present difficulties in processing as the amount of active substance is disproportionately small in relation to the carrier material (Voss col. 1, ll. 20-28).

FF11 Voss notes that "in pressing tablets of low-dosage active substances, the dissolution rate and consequently the resorption capacity of the active substance in the body are influenced in a negative way by unavoidable

sintering actions." (Voss col. 1, ll. 42-46.) Thus, Voss teaches, that at low dosages of active ingredients, the exact dosing of the active substance is especially important, and may be achieved "if the liquid, dissolved or suspended active substance is dotted onto the pharmaceutical carrier in a specific quantity in the form of discrete droplets of specific volume." (Voss col. 1, ll. 45-67.)

FF12 Thus, Voss recognizes that achieving a desired dosage of an active substance is related to the dissolution rate of the active substance.

FF13 Voss also provides an Example of dotting an edible pharmaceutical carrier, in which the label "comprised the name of the preparation, the dosage, and the taking time, was composed of 250 dots (one letter was formed from about 20 dots)." (Voss col. 6, ll. 62-65.) The label contained exactly 0.1mg of active substance (*id.* at ll. 65-68).

PRINCIPLES OF LAW

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The Supreme Court has recently emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). An "[e]xpress

suggestion to substitute one equivalent for another need not be present to render such substitution obvious." *In re Fout*, 675 F.2d 297, 301 (CCPA 1982). In addition, obviousness may be proved "by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the . . . claims." *KSR*, 127 S. Ct. at 1742.

ANALYSIS

According to the Examiner:

> Therefore, when creating a drug delivery substrate, it is Examiner's position that it would have been inherent for one of ordinary skill in the art to identify, in addition to a desired target dose, a target dissolution rate. The patterns of dots placed down on the delivery substrate of Voss would have been inherently placed to achieve said target dissolution rate for the safety and health of medical patients.
>
> One of ordinary skill in the art would have been well aware of the effects of surface area on dissolution rate, for example, that a plurality of small thin dots would dissolve faster than a thick, large dot. As evidence of this awareness, as outlined above, Voss teaches control of the parameters that would be known by ordinary artisans in the medical coating art to impact dissolution rate. Voss also recognizes the importance of dissolution rate in that the label on the carrier carries a "taking time" (see Example 2), i.e., a reminder to the patient that the effectiveness of the bioactive is about to wear off, and a new dose needs to be administered. This required knowledge of the dissolution rate of the bioactive, among other parameters.

(Ans. 4-5.)

Appellants assert that the "criteria for satisfying the requirements of 35 U.S.C. § 103 are intentionally strenuously high, precisely to prevent the trivial application of hindsight reconstruction of an otherwise patentable

invention." (App. Br. 8.) Appellants argue that there must be a specific teaching, suggestion, or motivation to modify the teachings of the prior art, and the Examiner "is merely asserting that such motivation must necessarily exist." (*Id.*) Such an assertion, Appellants assert, is not sufficient to establish a prima facie case of obviousness (*id.*). Moreover, Appellants argue, the Examiner may not rely on the level of ordinary skill in the art to provide the motivation to modify the prior art (*id.* at 9).

Appellants' arguments are not convincing. As noted in the previous section, the obviousness analysis can take into account the inferences and creative steps that a person of ordinary skill in the art would employ. Moreover, as noted by the Court in *KSR*, "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton." 127 S. Ct. at 1742. Both the Specification (FF2) and Voss (FF12) acknowledge the relationship between dissolution rate and dosing. As noted by the Examiner, when creating a drug delivery substrate, it would have been inherent for one of ordinary skill in the art to identify a target dissolution rate to achieve a desired target dose (Ans. 5). As Appellants have not provided any argument or evidence as to why the scientific reasoning of the Examiner was incorrect, we conclude that the burden of setting forth a prima facie case of obviousness has been met as to claim 1, and the rejection is affirmed as to those claims. As Appellants do not argue claims 3, 6, 7, 32, and 33 separately (App. Br. 9), the rejection is affirmed at to those claims as well.

As to claims 2, 8-10, 30, and 31, Appellants argue that the claims require that the placement of the drops partially overlap, so as to create a target dissolution rate (App. Br. 9). But as noted by the Examiner (Ans. 5-

6), Voss specifically provides an example in which the drops are placed in the form of letters, showing careful control of drop placement, and the suggestion of overlapping the drops to form the letters. Thus, again, Appellants' arguments are not convincing, and the rejection is affirmed as to claims 2, 8-10, 30, and 31 as well.

CONCLUSIONS OF LAW

We conclude that the Examiner has set forth a prima facie case that claims 1-3, 6-10, and 29-33 are obvious over Voss.

ISSUE (Obviousness over the combination of Voss and Voges)

Appellants contend that the Examiner has not set forth a prima facie case that claims 4 and 5 are obvious over the combination of Voss and Voges.

Thus, the issue on Appeal is: Has the Examiner set forth a prima facie case that claims 4 and 5 are rendered obvious by the combination of Voss and Voges?

FINDINGS OF FACT

FF14 Claims 4 and 5 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Voss and Voges (Ans. 7).

FF15 The Examiner relies on Voss as set forth above (Ans. 7, FF7-9). The Examiner notes that Voss does not teach the use of thermal ejection elements (Ans. 7).

FF16 The Examiner finds that piezoelectric ejection units and thermal ejection elements are "obvious variants that would have been known to an ordinary artisan." (Ans. 7.)

FF17 Voges is cited for teaching "a method of forming droplets of bioactive agent by using one of the two forms of inkjet printing, namely either piezoelectric ejection device or a thermal ejection device (3:62-66)." (Ans. 7.)

ANALYSIS

The Examiner concludes:

> Since Voss teaches printing precise drops of bioactive agent using a piezoelectric element, such as is used in inkjet printing, and Voges teaches that either the piezoelectric or thermal types of inkjet printing are suitable for forming precise droplets of bioactive agent, Voges would have reasonably suggested the use of a thermal element in the method of Voss. It would have been obvious to one of ordinary skill in the art to use the interchangeability teachings of Voges in the method of Voss to provide Voss with a suitable, successful alternative element for dosing dots in a precise manner.

(Ans. 7.)

Appellants first reiterate their arguments as to Voss (App. Br. 10), and those arguments are not found to be convincing for the reasons set forth above as to the rejection over Voss alone.

Appellants argue next that Voges teaches a hand-held dispenser of droplets of medication for inhalation, and similar to the apparatus of Voss, "the medication *dosage* may be carefully controlled by varying the number of droplets applied, but the reference provides no suggestion as to how to modify the medication dissolution rate." (App. Br. 11.) Appellants argue

further that "if the apparatus of Voges were modified so as to print onto a delivery substrate, . . . the modification would destroy the utility of the Voges dispenser for inhalation therapy." (*Id.*)

Appellants' arguments are not convincing. First, Voges was cited by the Examiner only for teaching the use of a thermal ejection device in an inkjet printer, as Voss only specifically teaches an inkjet printer using a piezoelectric ejection device (FF15). Note that "[i]f a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *KSR*, 127 S. Ct. at 1740.

Moreover, as discussed above as to the rejection over Voss, dosage is related to droplet size, and Voss teaches the formation of drops having a specific volume (FF7, FF11), which would then have a desired dissolution rate. Thus, the Examiner has set forth a prima facie case that claims 4 and 5 are obvious over the teachings of the combination of Voss and Voges.

CONCLUSIONS OF LAW

We conclude that the Examiner has set forth a prima facie case that claims 4 and 5 are rendered obvious by the combination of Voss and Voges, and the rejection is affirmed.

TIME LIMITS

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv) (2006).

AFFIRMED

cdc

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